PATENT
0512-1009-1

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of: Roland CHERIF CHEIKH

Appl. No.: New Group: Unknown

Filed: February 1, 2002 Examiner: Unknown

For: DEVICE FOR LOCAL ADMINISTRATION OF SOLID OR SEMI-SOLID FORMULATIONS AND DELAYED-RELEASE FORMULATIONS FOR PROPOSAL PARENTAL ADMINISTRATION AND PREPARATION PROCESS

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

February 1, 2002

Sir:

The following preliminary amendments and remarks are respectfully submitted in connection with the above-identified application.

IN THE CLAIMS

Please cancel claims 1-72.

Please add the following new claims:

--73. Solid delayed-release formulation, intended to be placed in a body, containing at least one active principle and a biodegradable excipient, characterized in that the excipient is a polylactide-glycolide (PLGA) copolymer, and in that the concentration of active principle is between 40 and 100%.

74. Delayed-release formulation according to Claim 73, characterized in that the concentration of active principle is between 50 and 100%.

75. Delayed-release formulation according to Claim 73, characterized in that it has a thin and elongated form with a diameter not exceeding 3mm.

76. Delayed-release formulation according to Claim 75, characterized by a diameter not exceeding 2 mm.

77. Delayed-release formulation according to Claim 75, characterized by a diameter of the order of 0.1 mm.

78. Delayed-release formulation according to Claim 73, characterized by a minimum length/diameter ratio of 10.

79. Delayed-release formulation according to Claim 73, characterized in that it contains an active principle of peptide or protein nature.

80. Solid delayed-release formulation for parenteral administration comprising a homogeneous mixture of an active principle in the non-dispersed state forming a continuous phase of which at least one part is in direct contact with the exchange

surface of the formulation and of the exterior biological medium, and of a biodegradable biocompatible excipient, in which the quantity of active principle is at least 50% by weight with respect to the total weight of the formulation, and having a release profile which is independent of the composition of the excipient, of the molecular weight of the excipient or of the active principle/excipient weight ratio, the release profile being essentially exclusively dependent on the total quantity of active principle present in the formulation.

81. Delayed-release formulation according to Claim 80, characterized in that the biodegradable biocompatible excipient is a polymer or copolymer of lactic and/or glycolic acid or a mixture of polymers and/or copolymers of lactic and/or glycolic acid.

82. Delayed-release formulation according to Claim 81, characterized in that the said biodegradable biocompatible polymer is a copolymer of lactic acid and glycolic acid (PLGA).

83. Delayed-release formulation according to Claim 80, characterized in that the said biodegradable biocompatible polymer is a copolymer of lactic and glycolic acid having an intrinsic viscosity in chloroform at 1 g per 100 ml of greater than 0.6 dl/g.

84. Delayed-release formulation according to Claim 82,

characterized in that the copolymer of lactic acid and glycolic acid is of hydrophilic nature.

85. Delayed-release formulation according to Claim 80, characterized in that, when it is placed *in vitro* in a physiological liquid medium, it liberates almost the whole of the active principle in less than a week, and, when it is placed *in vivo* subcutaneously or intramuscularly, has a release of active principle over a period substantially greater than one week.

86. Delayed-release formulation according to Claim 80, characterized in that it comprises a mixture of the active principle and the excipient which is homogenous at all points.

87. Delayed-release formulation according to Claim 80, characterized in that the release takes place in a single diffusion phase of the active principle.

88. Delayed-release formulation according to Claim 80, characterized in that the active principle represents at least 51%, advantageously at least 60%, preferably at least 70% and up to 99.999% by weight with respect to the total weight of the formulation, the excipient representing less than 50%, preferably less than 49%, and more advantageously less than 30% by weight with respect to the total weight of the formulation.

89. Delayed-release formulation according to Claim 80, characterized in that the active principle is a peptide, a peptide analogue or a protein, especially LHRH or an analogue of LHRH, especially Triptoreline.

90. Delayed-release formulation according to Claim 80, characterized in that it is in cylindrical form and has a diameter less than or equal to 3 mm, preferably less than 1 mm.

91. Delayed-release formulation according to Claim 80, for injection by the intramuscular or subcutaneous route.

92. Delayed-release formulation according to Claim 80, characterized in that it is in the form of an implant.

93. Process for preparation of a delayed-release formulation according to Claim 80, comprising the steps consisting in:

- producing a homogeneous mixture of the active principle and the excipient, containing at least 50% of active principle;
- compacting the said mixture; and
- extruding the said compacted mixture in the molten state.

94. Process for preparation of a formulation according to Claim 80, comprising the steps consisting in:

- producing a homogeneous mixture of the active principle and the excipient, containing at least 50% of active principle;

- subjecting the homogeneous mixture of a high compression;

- grinding the compressed articles obtained; and

- putting into a form suitable for administration.--

REMARKS

Claims 73-94 are pending in the present application.

Entry of the above amendments is earnestly solicited. An early and favorable first action on the merits is earnestly requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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